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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,497	01/18/2002	Rong-Hwa Lin	13062-003001	1774
26161	7590	04/25/2005	EXAMINER	
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			1644	

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/051,497

Applicant(s)

LIN ET AL.

Examiner

Phillip Gambel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,6-13,17,19,20 and 22-25 is/are pending in the application.
- 4a) Of the above claim(s) 7-9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,6,10-13,17,19,20 and 22-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's amendment, filed 1/25/05, has been entered.
Claims 1, 3, 4, 11-13, 17, 19, 20 and 23-25 have been amended.
Claims 2, 5, 14-16, 18, 21, and 26-37 have been canceled.

Claims 1, 3, 4, 6-13, 17, 19, 20 and 22-25 are pending.

As pointed out previously, applicant's election of species (B), drawn to methods using an anti-PSGL-1 antibody and an agent that binds to the antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the cell surface without traverse in the Reply, filed 7/22/04, and the species autoimmune disease and type I diabetes in the Reply, filed 3/10/04, has been acknowledged.

Claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22, 23, 24 and 25 are under consideration in the instant application.

Claims 7-9 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected invention or species.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's amendment, filed
The rejections of record can be found in the previous Office Action.
3. As indicated previously, the filing date of the instant claims is deemed to be the filing date of the instant application USSN 10/051,497, filed 8/3/01, as the previous provisional priority application does not appear to provide sufficient written description for the claimed "limitations".

Applicant's amendment, filed 1/25/05, does not indicate any disagreement with the priority date of the instant application.

Again, if applicant disagrees, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the parent application. Applicant is invited to verify the priority date of the instant claims, including written support and enablement under 35 USC 112, first paragraph.

4. Applicant's amended claims, filed 1/25/05 have obviated the previous rejections under 35 U.S.C. § 112, first paragraph, written description with respect to "a compound that binds to PSGL-1" and "an agent that binds to the monoclonal antibody".
5. Applicant's amended claims have obviated the previous rejection under 35 U.S.C. § 112, first paragraph, scope of enablement with respect to "a compound that binds to PSGL-1"
6. Applicant's amended claims have obviated the previous rejection under under 35 U.S.C. § 112, first paragraph, scope of enablement with respect to the recitation of "preventing"

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7. This is a rejection under 35 USC § 112, first paragraph, "new matter".

Claims 4 and 20 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed:

"an antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigen on the surface of the T cell".

Applicant's amendment, filed 1/25/05, directs support to various pages in the specification as filed.

However, it appears that applicant is relying upon the disclosure of the anti-hamster Ig as a cross-linker antibody (e.g. see Example 3 on pages 19-20) to support an entire genus of "antibodies that bind to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigen on the surface of the T cell".

Other than that, the specification discloses "agents that bind to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of cell" (e.g. see Summary of the Invention, particularly page 5, paragraph 3 of the instant specification).

Applicant's reliance on a generic disclosure (e.g. agent) and possibly a single or limited species (e.g. anti-hamster Ig in an Example) does not provide sufficient direction and guidance to the generic "antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigen on the surface of the T cell", as currently claimed.

It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

The specification as filed does not provide a sufficient written description nor provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitation", as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above. See MPEP 714.02 and 2163.06

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8. Claims 4 and 20 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling "anti-hamster Ig" and "rabbit anti-mouse Ig" as "an antibody that bind to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of cell",

does not reasonably provide enablement for any "antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of T cell".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.
molecule

Applicant appears to be relying upon the disclosure of the anti-hamster Ig or rabbit anti-mouse Ig as a cross-linker antibody (e.g. see Example 3 on pages 19-20 and Example 10 on pages 26-27) to support an entire genus of "antibodies that bind to an anti-PSGL-1 antibody".

This invention encompasses any "antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of cell" (e.g. see Summary of the Invention, particularly page 5, paragraph 3 of the instant specification), yet the instant specification does not provide sufficient direction and guidance as to the nature of antibodies that can induce cross-linking in vivo, broadly encompassed by the claimed invention.

While cross-linking antibodies in vivo may be accomplished by various antibody constructs, including multimeric antibodies, or antibodies that bind anti-PSGL antibodies that are not hamster antibodies, the instant disclosure provides for insufficient guidance and direction towards the relevant, identifying characteristics of the "antibodies that bind to an anti-PSGL-1 antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of T cell".

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any "antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigens on the surface of T cell, other than "anti-hamster antibody".

Without sufficient guidance, making and using an "antibody that binds to the monoclonal antibody and induces the cross-linking of plurality of PSGL-1 antigens on the surface of T cell" other than the "anti-hamster/mouse Ig" disclosed in the specification as filed as the "antibody" in the claimed methods would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

9. Applicant's amended and canceled claims, filed 1/25/05, have obviated the previous objections and rejections under 35 U.S.C. § 112, second paragraph,

10. As pointed out previously, for examination purposes, it appears that claimed methods which rely upon the elected species of administering an anti-PSGL-1 antibody and an "agent that binds to the monoclonal antibody and induces the cross-linking of plurality of PSGL-1 antigens on the surface of T cell appears free of the prior art.

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Accordingly, the prior art rejections have been extended to read on the species of administering anti-PSGL-1 antibodies in the absence of administering a secondary "cross-linking agent".

As indicated in the prior art rejections that follow, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosures of administering anti-PSGL-1 antibodies to inhibit P-selectin- / PSGL-1-mediated interactions, including immune responses such as the elected autoimmune disease diabetes.

However, the prior art disclosures are silent on the claimed recitation of "inducing a signal transduction pathway that results in the death of a T cell or NK cell".

As pointed out above, the Office is not equipped to conduct comparisons. Applicant is invited to provide clarity and objective evidence as to the mechanism of action by which the administration of anti-PSGL-1 antibodies can reduce T cell mediated immune responses, including autoimmunity such as diabetes in the absence of a secondary cross-linking agent.

11. Claims 1, 3, 6, 10-12, 17, 19 and 22-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Larsen et al. (U.S. Patent No. 5,840,679) (see entire document) essentially for the reasons of record.

Applicant' arguments, filed 1/25/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the prior art is drawn to the use of antagonistic anti-PSGL-1 antibodies, while the instant claims are drawn to the use of agonistic antibodies.

However, the claims nor the specification make it clear that the instant antibodies are necessarily agonistic antibodies and agonistic in terms of what endpoints, while the prior art taught antagonistic antibodies.

It is unclear how applicant is making this distinction, given that the claims rely upon anti-PSGL antibodies with no mention of agonistic properties and both the instant and prior art anti-PSLG-1 antibodies are administered to inhibit T cell mediated immune responses.

The reduction of T cell mediated immune responses may occur via multiple modes of action.

While applicant relies upon in vitro analysis and cross-linking of anti-PSGL antibodies under in vitro experimental conditions to show evidence of apoptosis, applicant does not provide objective evidence that the administration of anti-PSGL antibodies in vivo does or does not require cross-linking to achieve the decrease in T cell numbers and T cell mediated immune responses in view of antibody treatment of an experimental autoimmune diabetes model (see instant Example 11).

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While the invention may be based on the discovery that T cells can be depleted and/or induced to undergo apoptosis by the engagement of the T cell surface antigen PSGL (e.g. Summary of the Invention and applicant's arguments),

There is insufficient objective evidence that the treatment of anti-PSGL-1 antibodies in the prior art do not result in cross-linking (e.g. via Fc- FcR binding) and the claimed cell death of T cells.

Alternatively, while Example 11 discloses the use of anti-PSGL-1 antibodies to treat an experimental model of diabetes, there is insufficient objective evidence that the reduction of T cell mediated immune response is accomplished via the death of the T cells.

Although the reference is silent about the induction of T cell or NK cell death as well as identifying the T cell as activated, CD3⁺, CD4⁺, or CD8⁺ as well as the depletion of T cells, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

The products employed in the instant methods and the prior art are defined in terms of anti-PSGL-1 antibodies. Comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons

Applicant is invited to clarify the distinctions between the properties of anti-PSGL-1 antibodies and the instant anti-PSGL-1 antibodies and claimed the antibodies accordingly.

At this time, it is difficult for the examiner to determine whether applicant has discovered a new mode of action (e.g. induction of apoptosis) of anti-PSGL-1 antibodies,

whether applicant has discovered a new epitope specificity of apoptosis-inducing anti-PSGL-1 antibodies,

whether applicant is relying upon secondary cross-linking agents / antibodies to accomplish this newly discovered mode of action and/or

whether the administration of anti-PSGL-1 antibodies even in applicant's model operate via apoptosis in vivo in the absence of secondary cross-linking agents / antibodies.

Therefore the prior art stands at this time, given it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

See the previous Office Action for a more complete analysis of the prior art rejection.

12. Claims 1, 3, 6, 10-13, 19, 20, 22, 23, 24 and 25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over by Larsen et al. (U.S. Patent No. 5,840,679) in view of Trembleau et al. (J. Immunol. 163 : 2960 – 2968, 1999), Yago et al. (J. Immunol. 161 : 1140 – 1145 (1998), Hirata et al. (J. Exp. Med. 192: 1669 – 1675, 2000) and Cobbold et al. (U.S. Patent No. 6,056,956) essentially for the reasons of record.

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Applicant's arguments, filed 1/25/05, and the examiner's rebuttal are essentially the same set forth above.

Therefore, applicant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

See the previous Office Action for a more complete analysis of the prior art rejection.

13. No claim allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, PhD.
Primary Examiner
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April 18, 2005